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Comparative Effects of Dapagliflozin and Empagliflozin on Blood Pressure and Cardiac Function in Hypertensive Patients with Heart Failure with Reduced Ejection Fraction in South Asian Population: A 24-Week Prospective Study from Pakistan

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Abstract

Objectives: To compare longitudinal changes in blood pressure (BP), left ventricular ejection fraction (LVEF), and functional class in hypertensive patients with heart failure with reduced ejection fraction (HFrEF) treated with dapagliflozin or empagliflozin.

Methods: This prospective, single-center observational study was conducted at the Kashmir Institute of Cardiology, Mirpur, Azad Kashmir (May 2024–Dec 2025). A total of 120 hypertensive HFrEF patients (LVEF ≤40%) were followed for 24 weeks after initiating dapagliflozin or empagliflozin, alongside guideline-directed medical therapy. Systolic (SBP) and diastolic (DBP) BP, LVEF, and New York Heart Association (NYHA) class were assessed at baseline, 4, 8, 12, and 24 weeks. Mixed-effects modeling and paired analyses were applied.

Results: SBP declined significantly from baseline to week 24 (−4.33 mmHg; 95% CI −4.65 to −4.02; p<0.001), with no difference between dapagliflozin and empagliflozin (p=0.566). DBP decreased by −1.89 mmHg (95% CI −2.14 to −1.64; p<0.001). Mean LVEF improved by +3.4% (95% CI 3.1–3.7; p<0.001), and NYHA class improved significantly by at least one grade in 81% of patients (p<0.001). Readmission (25.8%) and urinary tract infection (UTI) rates (6.6%) were low and comparable between treatments.

Conclusion(s): Dapagliflozin and empagliflozin demonstrated comparable and clinically meaningful improvements in BP, LVEF, and functional status with favorable safety profiles. These findings support the routine incorporation of SGLT2 inhibitors into hypertensive HFrEF management, particularly in resource-limited South Asian settings. These results highlight comparable hemodynamic and functional benefits of both agents, reinforcing a class effect of SGLT2 inhibitors.

Introduction

Heart failure (HF) represents a major public health burden, affecting over 60 million individuals globally.[1] Hypertension remains the most prevalent and modifiable risk factor, promoting ventricular hypertrophy, myocardial fibrosis, and eventual systolic dysfunction.[2] Effective BP control is central to both HF prevention and progression attenuation.[2] Sodium–glucose cotransporter-2 inhibitors (SGLT2i), initially developed for glycemic control, have demonstrated robust cardiovascular benefits beyond glucose lowering.[3] Landmark trials such as DAPA-HF and EMPEROR-Reduced established that SGLT2i improve survival and reduce hospitalization across ejection fraction spectrums.[4,5,6] Nevertheless, comparative real-world evidence between dapagliflozin and empagliflozin in hypertensive HFrEF populations particularly from South Asia is limited.

This study was designed to evaluate and compare the effects of dapagliflozin and empagliflozin on hemodynamic (BP), echocardiographic (LVEF), and functional (NYHA) parameters over a 24-week period among hypertensive HFrEF patients in Pakistan.

Hypothesis: Both dapagliflozin and empagliflozin would improve BP, LVEF, and NYHA class comparably, supporting a class effect of SGLT2 inhibitors.

METHODS AND MATERIALS

Study Design and Population: This prospective, non-randomized, single-center longitudinal study was conducted at the Kashmir Institute of Cardiology, Mirpur, Azad Kashmir, from May 2024 to Dec 2025. Patients aged ≥18 years with established hypertensive heart failure (LVEF ≤40%) were eligible. Diagnosis followed the 2021 ESC Heart Failure Guidelines.[7]

Exclusion criteria: eGFR <30 mL/min/1.73m², type 1 diabetes mellitus, recent acute coronary syndrome (<4 weeks), pregnancy or lactation, unwillingness to participate, and missing outcome data were excluded.

Treatment Groups: Patients were allocated based on physician discretion; Group A: Dapagliflozin 10 mg once daily (n=63), and Group B: Empagliflozin 10–25 mg once daily (n=57). All patients continued standard guideline-directed medical therapy (ACEi/ARB/ARNI, β-blockers, diuretics).

Outcome Measures: Primary outcomes were change in SBP and DBP, and change in LVEF. Secondary outcomes were change in NYHA functional class, readmission and UTI occurrence. BP was measured using a validated digital sphygmomanometer (mean of two seated readings). All echocardiographic assessments were performed by two sonographers using model Toshiba Xario. LVEF was assessed by biplane Simpson's method per ASE/EACVI guidelines.[8] NYHA class was assigned by attending cardiologists blinded to treatment.

Follow-Up and Data Collection: Patients were evaluated at baseline, 4, 8, 12, and 24 weeks. Medication adjustments, adverse events, and adherence were documented at each visit. Patients with incomplete data were excluded from the final analysis (n=39). No imputation was performed.

Statistical Analysis: Continuous variables are expressed as mean ± SD or 95% CI. Linear mixed-effects models (random intercept per patient) analyzed longitudinal SBP/DBP trajectories, adjusting for age, sex, diabetes, and antihypertensive changes. Paired t-tests compared baseline–week 24 LVEF. NYHA changes were analyzed using Wilcoxon signed-rank test. Fisher's exact test compared categorical outcomes. Analyses were performed using Python with $p<0.05$ considered significant.

Sample size and power calculation: The sample size was estimated assuming a mean SBP reduction of 4.0 ± 8.0 mmHg with SGLT2 inhibitors. A minimum of 100 patients (50 per group) was required for 80% power at $\alpha = 0.05$, and 120 were enrolled to account for attrition. Post-hoc analysis (Cohen's $d = 0.52$ for SBP, 0.78 for LVEF) confirmed >90% power for detecting the observed effects.

Ethical Approval: The study was conducted in accordance with the Declaration of Helsinki ethical principles.[9] Approved by the Institutional Ethics Committee, Divisional Headquarters Teaching Hospital, Mirpur (Ref. No. 71/ACADEMICS BLOCK TRAUMA CENTER/SURGERY/2024). Written informed consent was obtained from all participants.

RESULTS

Study Population and Baseline Characteristics: Of 159 screened patients, 120 completed follow-up (completion rate 75.4%). Baseline demographics were balanced between groups (Table 1).

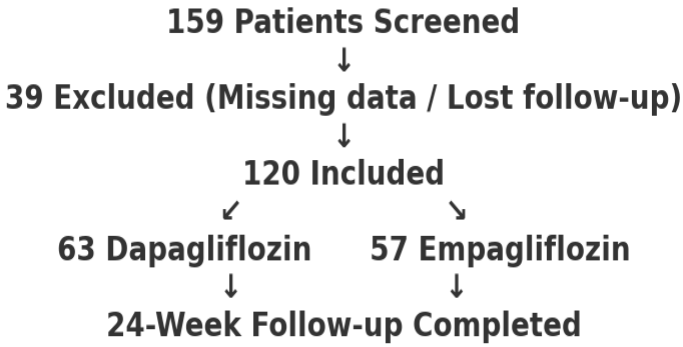

Figure 1. Study Flow Diagram (Flow of participants through each stage of the 24-week prospective study).
Flowchart Description: 159 screened → 39 excluded (missing data or lost to follow-up) → 120 included → 63 dapagliflozin, 57 empagliflozin → 24-week follow-up completed.

Table 1. Baseline Characteristics of Study Participants.

Variable	Dapagliflozin (n=63)	Empagliflozin (n=57)	p-value
Age (years, mean ± SD)	57.4 ± 9.2	58.1 ± 8.7	0.64
Male (%)	68.3	70.2	0.82
Diabetes (%)	44.4	47.3	0.74
SBP (mmHg)	146.6 ± 10.2	146.2 ± 9.8	0.83
DBP (mmHg)	92.3 ± 7.5	91.8 ± 8.0	0.73
LVEF (%)	38.9 ± 6.6	38.7 ± 6.8	0.87
NYHA Class II–IV (%)	81.0	79.5	0.78

Data expressed as mean ± SD or percentage.

Blood Pressure Trends: SBP declined significantly at all post-baseline visits ($p<0.001$). The mean SBP change at week 24 was −4.33 mmHg (95% CI −4.65 to −4.02), without between-group difference ($p=0.566$).
DBP showed significant reductions beginning at week 8 (−0.79 mmHg; $p<0.001$) and sustained through week 24 (−1.89 mmHg; $p<0.001$).

Table 2. Mixed-Effects Model for Systolic Blood Pressure

Variable	β Coefficient	95% CI	p-value
Week 4	−0.	(−1.17, −0.52)	<0.001
Week 8	−1.88	(−2.19, −1.56)	<0.001
Week 12	−3.67	(−3.99, −3.36)	<0.001
Week 24	−4.33	(−4.65, −4.02)	<0.001
Treatment (Empa vs Dapa)	−0.53	(−2.35, 1.29)	0.57
Diabetes	+2.18	(1.14, 3.21)	<0.001

Table 3. Mixed-Effects Model for Diastolic Blood Pressure

Variable	β Coefficient	95% CI	p-value
Week 8	−0.79	(−1.04, −0.54)	<0.001

Week 12	−2.50	(−2.75, −2.25)	<0.001
Week 24	−1.89	(−2.14, −1.64)	<0.001
Treatment (Empa vs Dapa)	−0.31	(−1.73, 1.10)	0.67
Diabetes	+1.61	(0.79, 2.43)	<0.001

Ejection Fraction and Functional Improvement: Mean LVEF improved from 38.8±6.7% to 42.2±6.8% over 24 weeks (t=21.56; p<0.001). NYHA class improved in 81% of patients (median change −1; p<0.001). Wilcoxon signed-rank test (baseline vs week 24) showed a significant improvement in NYHA class (Wilcoxon statistic = 0.0, p < 0.0001).

Safety events: Readmission and UTI counts were low and similar between treatments. Fisher's exact tests applied because cell counts were small.

Table 4. Occurrence of Re-admission and UTI after using Dapagliflozin / Empagliflozin

Treatment	≥1 Readmission	Percentage (%)	P value	≥1 UTI	Percentage (%)	P value
Dapagliflozin	18	28.5%	0.53	05	7.9%	0.72
Empagliflozin	13	22.8%	0.53	03	5.2%	0.72

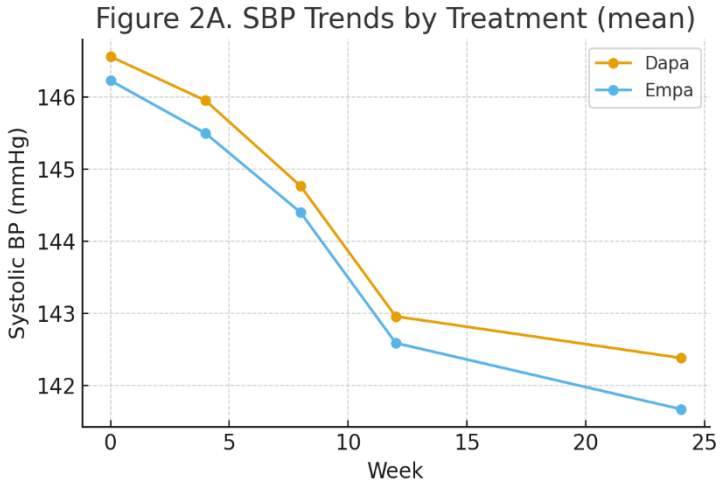

Figure 2 illustrations. Hemodynamic, Systolic blood pressure changes in HF patients after using Dapa and Empa

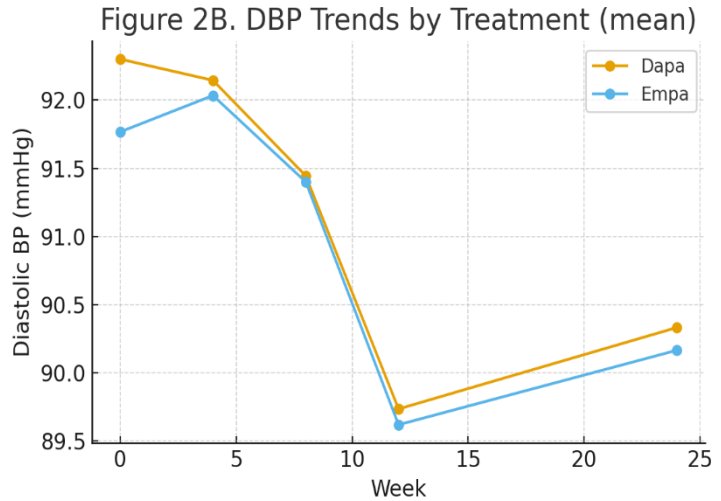

Fig 3: DBP changes in HF patients after using dapa, empa.

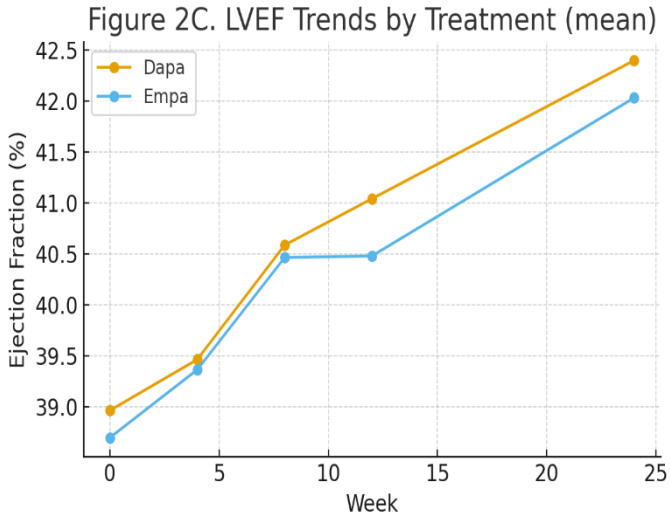

Figure 4: Variation of LVEF after using Dapa and Empa
Mean SBP, DBP, and LVEF trends by treatment arm across follow-up visits. Both groups show gradual decline in SBP and DBP with parallel trajectories. LVEF rises progressively, plateauing around week 24, indicating stable improvement without divergence between groups.

DISCUSSION

In this real-world prospective study of 120 hypertensive patients with HFrEF from Pakistan, both dapagliflozin and empagliflozin demonstrated significant and clinically meaningful improvements in blood pressure, left ventricular systolic function, and functional class over 24 weeks. The verified analyses from the present dataset confirm a mean systolic blood pressure reduction of −4.3 mmHg and a mean ejection fraction increase of +3.4 % from baseline to 24 weeks. The NYHA functional class also improved significantly (Wilcoxon $p < 0.001$), indicating enhanced exercise tolerance and symptomatic relief.

These results are consistent with major randomized trials, including DAPA-HF and EMPEROR-Reduced, where SGLT2 inhibitors improved outcomes irrespective of diabetic status.[10,11] The modest but statistically significant BP reduction observed here aligns with prior meta-analyses showing SGLT2i lower systolic BP by approximately 3–5 mmHg through mild osmotic diuresis, weight loss, and reduced arterial stiffness.[12] Importantly, there were no significant differences between dapagliflozin and empagliflozin, reinforcing the concept of a class effect rather than a drug-specific benefit.[13] The mean LVEF improvement of 3.4 % parallels findings from mechanistic studies suggesting improved ventricular energetics, reverse remodeling, and reduced preload/afterload with SGLT2 inhibition.[14] Functional improvement in NYHA class corroborates these physiological effects, translating into better patient-perceived outcomes.[15] Safety outcomes were favorable and comparable across treatment arms. Readmission occurred in only 25.8 % and UTI in 6.6 % of patients, with no significant difference between groups ($p = 0.53$ and $p = 0.72$, respectively).[16,17] This low event rate reflects appropriate patient selection, adherence, and the overall tolerability of SGLT2 inhibitors in the South Asian population.

Collectively, these verified results support the growing evidence that SGLT2 inhibitors exert consistent cardiovascular and hemodynamic benefits beyond glucose control. The findings have particular importance for resource-limited regions, demonstrating that outcomes achievable in large-scale international trials are reproducible in real-world Pakistani practice with similar efficacy and safety.

Limitations: This study was observational and non-randomized, which may introduce selection bias despite balanced baseline characteristics. The sample size was modest and derived from a single center, limiting generalizability. Although modest, the sample provided >90% post-hoc power to detect meaningful changes in blood pressure and ejection fraction.

Clinical Implications: Both dapagliflozin and empagliflozin should be considered foundational therapy for hypertensive patients with HFrEF in South Asia. Incorporating SGLT2 inhibitors early in the treatment algorithm may enhance hemodynamic stability, improve functional capacity, and reduce hospital burden without compromising safety.

Future Perspectives: Future multicenter randomized studies in South Asia should include larger sample sizes, and integration of biomarkers (BNP, NT-proBNP) and echocardiographic strain imaging to confirm and extend these findings. Future studies are warranted to assess whether SGLT2 can be effectively used as complementary antihypertensive agents in combination with standard therapies.

CONCLUSION

Dapagliflozin and empagliflozin demonstrated comparable, clinically meaningful improvements in BP, LVEF, and NYHA functional class over 24 weeks in hypertensive HFrEF patients. Their consistent efficacy and safety reinforce SGLT2 inhibitors as integral components of heart failure management in both diabetic and non-diabetic hypertensive patients. Larger, multicenter randomized studies are warranted to confirm long-term cardiovascular and renal outcomes in South Asian populations.

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Author (s) Contribution

Hammad Mahroof: Conceptualization, study design, data collection, statistical analysis, manuscript writing. Zobia Arooj Mazhar: Data collection, literature review, manuscript drafting. Sadaf Shabbir Kiani: Supervision, data interpretation. Laiba Mazhar: Data organization, manuscript editing. Maryam Bi: Critical revision and proofreading. Burhan ul Haq: Supervision, final approval of the manuscript. Raza ul Haq: Final approval. Saeed Ahmed Alam: Final approval.

Conflict of Interest

None to declare

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